

3. Remarks

This Amendment and Reply is filed in response to the final Office Action having a mailing date of January 2, 2003. Claims 15-34 are currently pending in the application with claims 15, 29, 30, 31 and 32 being in independent form. Applicants wish to add claims 35-39.

- Support for claim 35: fragments of the extracellular domain (amino acids 123-285 and 73-285 of SEQ ID NO:4) may be found at page 7, lines 1-6 and support for Fc fusions may be found in Examples 1-5.
- Support for claim 36: amino acids 123-285 of SEQ ID NO:4 may be found at page 7, lines 5-6.
- Support for claims 37-39: human antibodies, Fab fragments and F(ab')₂ fragments may be found at page 9, lines 21-26.

Claims 15-34 stand rejected under 35 U.S.C. §112, first paragraph for lack of enablement. Claims 15-34 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite. Claims 15, 19, 20, 23, 25 and 29-34 are rejected under 35 U.S.C. §103(a) as being unpatentable over *Chaudhary* in view of *Bringman* and *Bram*. Applicants will address each of these issues in the order presented in the Office Action.

1. 35 U.S.C. §112, first paragraph

The Examiner asserts that the specification does not reasonably provide enablement for a polypeptide encoded by a nucleic acid molecule 75% identical to SEQ ID NO:1 or 3. Applicants have amended the claims to recite 90% variants and incorporate the previous arguments of record as support. Support for the 90% variants may be found at page 6, line 7.

2. 35 U.S.C. §112, second paragraph

The Examiner has rejected claims 15-34 under 35 U.S.C. §112, first paragraph on the basis that the specification does not reasonably provide enablement for "TACI" and "TACI-L." Applicants have amended the claims to delete reference to "TACI" and "TACI-L" and refer to the various polypeptides used in the screening assays in terms of amino acid sequences disclosed in SEQ ID NO:2 and 4. Support for amino acids 73-285

and 123-285 of SEQ ID NO:4 may be found at page 7, lines 1-6. Support for amino acids 2-166 of SEQ ID NO:2 may be found at page 12, line 16.

All pending claims have been amended to delete reference to "TACI" and TACI-L" and to refer to the polypeptides by SEQ ID NO:2 and 4, respectively. As such, Applicants request the rejections under 35 U.S.C. §112, second paragraph be withdrawn.

3. 35 U.S.C. §103(a)

The Examiner has maintained his rejection of claims 15, 19, 20, 23, 25 and 29-34 under 35 U.S.C. §103(a) as being unpatentable over *Chaudhary* in view of *Bringman* and *Bram* for reasons of record. Applicants respectfully traverse.

Applicants respectfully submit that the Patent Office has not set forth a *prima facie* case of obviousness because the Patent Office has failed to provide the "clear and convincing" evidence showing the requisite suggestion, teaching or motivation to combine the cited references. (The following discussion refers to SEQ ID NO:2 as TACI and SEQ ID NO:4 as TACI-L.)

In April of 1999 it was not known that TACI and TACI-L were cognates – this relationship was first discovered by Applicants and forms the basis for the claimed invention. The Federal Circuit has established that "[o]bviousness cannot be predicated on what is not known at the time an invention is made, even if the inherency of a certain feature is later established." *In re Rijckaret*, 9 F.2d 1531, 28 USPQ 1955 (Fed. Cir. 1993). In other words, what was not known in the art at the time of filing cannot be considered obvious later on. It is indisputable that the claimed invention was unknown at the time of filing and therefore cannot be considered obvious in hindsight.

Chaudhary discloses the DNA and protein sequences for TACI-L (TNRL1- α) and teaches that TACI-L binds to BJAB cells and has a negative impact on cell survival. *Bram* discloses the DNA and protein sequences for TACI and teaches that TACI is expressed on B-cells. *Chaudhary* and *Bram* do not suggest or teach in any way that their respective proteins specifically bind to the other or provide the requisite motivation to develop a screening assay based on the specific interaction of TACI and TACI-L. To establish a *prima facie* case of obviousness, it is essential that "[t]he teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure." *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1439 (Fed. Cir. 1991). At the time of filing the present application, there was not an established nexus between the teachings of

Chaudhary and *Bram* and a skilled artisan would have no reason to combine the two teachings. In addition, neither *Chaudhary* nor *Bram* make any suggestion that their discoveries are related in any way. Therefore, one of skill in the art would not have a reasonable expectation of success of developing screening methods based on the specific interaction of TACI and TACI-L until it was clearly and unambiguously established that TACI and TACI-L were a specific receptor:ligand pair. In the present case, it is the Examiner – not the cited art – who has provided the suggestion to make the claimed combination and the reasonable expectation of success. Therefore, the Patent Office has not met the legal standard for establishing *prima facie* obviousness.

The Examiner asserts that it would have been obvious to one of skill in the art to make a neutralizing antibody against TACI-L and test the antibody in the BJAB assay to see if it affects cell survival. Applicants respectfully note that this is not the claimed invention. Applicants are not claiming a method of screening a test compound by assaying for the level of interaction between TACI-L and an unidentified protein on BJAB cells. In contrast, Applicants are claiming a method of screening a test compound by assaying for the level of interaction between TACI and TACI-L. None of the cited art references teach or suggest the specific interaction of TACI and TACI-L.

Bringman has been cited to show that neutralizing antibodies, in the most generic sense, were known in the art. *Bringman* has no connection whatsoever to *Chaudhary* or *Bram*. The antibodies described in *Bringman* are not particular to TACI or TACI-L. There is no suggestion or motivation in *Chaudhary*, *Bram* or *Bringman* to combine the prior art references to make the claimed invention. Therefore, the motivation to combine the references has been provided by the Examiner.

In addition, Applicants submit that part of the Examiner's reasoning is based on unsupported conclusory statements rather than clear and particular evidence required by the Federal Circuit. And, the Examiner has improperly shifted the burden of proof onto Applicants to show the Examiner's assumptions have a basis in fact. The Examiner assumes that the unidentified receptor on the BJAB cells described in *Chaudhary* is TACI and requires Applicants to prove otherwise. Applicants note that "The initial burden is on the Examiner to provide some suggestion of the desirability of doing what the inventor has done" (MPEP §2142). There is no evidence in any of the cited art that suggests the specific relationship between TACI and TACI-L and consequently there is no particular motivation to develop methods of screening based on TACI and TACI-L. With regards to the observation reported in *Chaudhary*, Applicants submit that merely showing that

that TACI-L (TNRL1- α) binds to a B-cell line (BJAB) does not unequivocally identify the TACI protein as the receptor for TACI-L, which is necessary to render the claimed invention obvious.

The law is clearly on Applicants' side in this matter. The court in *In re Dembiczak*, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999) stated that evidence of a suggestion, teaching, or motivation to combine may flow from the prior art references themselves, the knowledge of one of ordinary skill in the art, or, in some cases, from the nature of the problem to be solved. The range of sources available, however, does not diminish the requirement for actual evidence. That is, the showing must be clear and particular. See, e.g., *C.R. Bard*, 157 F.3d at 1352, 48 USPQ2d at 1232. Broad conclusory statements regarding the teaching of multiple references, standing alone, are not "evidence." E.g., *McElmurry v. Arkansas Power & Light Co.*, 995 F.2d 1576, 1578, 27 USPQ2d 1129, 1131 (Fed. Cir. 1993). The Federal Circuit has made clear that the showing must be by clear and convincing evidence. *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 57 USPQ2d 1449 (DC Mass 2001).

It is well established that "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). Applicants respectfully submit that a conclusion of *prima facie* obviousness must be supported by *evidence*, a showing by some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references to arrive at the claimed invention. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). "A rejection cannot be predicated on the mere identificationof individual components of claimed limitations. Rather, particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed." *In re Kotzab*, 217 F.3d 1365, 1369, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000).

The *Dembiczak* court further stated that a reference-by-reference, limitation-by-limitation analysis does not demonstrate how the prior art references teach or suggest their combination to yield the claimed invention. Also, the court in *In re Rouffet* reiterated the fact that "virtually all [inventions] are combinations of old elements." *In re Rouffet*, 149 F.3d 1350, 47 USPQ2d 1453 (Fed. Cir. 1998), see also *Environmental Designs, Ltd. v. Union Oil Co.*, 713 F.2d 693, 698, 218 USPQ 865, 870 (Fed. Cir. 1983);

and *Richdel, Inc. v. Sunspool Corp.*, 714 F.2d 1573, 1579-80, 219 USPQ 8, 12 (Fed. Cir. 1983) ("Most, if not all, inventions are combinations and mostly of old elements."). Therefore an examiner may often find every element of a claimed invention in the prior art. If identification of each claimed element in the prior art were sufficient to negate patentability, very few patents would ever issue. Furthermore, rejecting patents solely by finding prior art corollaries for the claimed elements would permit an examiner to use the claimed invention itself as a blueprint for piecing together elements in the prior art to defeat the patentability of the claimed invention. Such an approach would be "an illogical and inappropriate process by which to determine patentability." *In re Rouffet, supra*, see also *Sensonics, Inc. v. Aerosonic Corp.*, 81 F.3d 1566, 1570, 38 USPQ2d 1551, 1554 (Fed. Cir. 1996).

Applicants readily acknowledge that the claimed invention is to a certain extent a combination of elements already known in the art (i.e., TACI and TACI-L), but this is not sufficient grounds for finding obviousness ("virtually all [inventions] are combinations of old elements." *In re Rouffet, supra*). In general, the Examiner has found the individual elements of Applicants' claimed invention in the prior art, or at least prior art corollaries (i.e., *Bringman*). But, "[I]f identification of each claimed element in the prior art were sufficient to negate patentability, very few patents would ever issue. Furthermore, rejecting patents solely by finding prior art corollaries for the claimed elements would permit an examiner to use the claimed invention itself as a blueprint for piecing together elements in the prior art to defeat the patentability of the claimed invention." *In re Rouffet, supra*). Applicants suggest this is precisely what has occurred.

Applicants respectfully submit that the only suggestion for the Examiner's combination of the isolated teachings of the applied references improperly stems from Applicants' disclosure. It is impermissible to use the claimed invention as an instruction manual or "template" to piece together the teachings of the prior art so that the claimed invention is rendered obvious. *In re Gorman*, 933 F.2d 982, 987, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991). "Determination of obviousness cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention." *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 546, 48 USPQ2d 1321, 1329 (Fed. Cir. 1998).

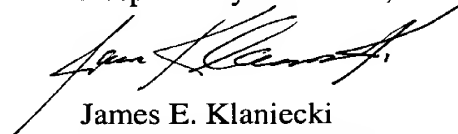
Finally, Applicants further note that a high level of skill in the art alone cannot be relied upon to provide motivation to combine prior art references in a manner that would render the claimed invention obvious. *In re Rouffet*, 47 USPQ2d 1453 (CAFC Jul. 15,

1998). The fact that the claimed invention is within the capabilities of one of ordinary skill in the art is not sufficient by itself to establish *prima facie* obviousness. *Ex parte Levengood*, 28 USPQ2d 1300 (BPAI, 1993); MPEP 2143.01.

Based on the above arguments, Applicants respectfully request the rejection of claims 15, 19, 20, 23, 25 and 29-34 under 35 U.S.C. §103(a) be properly withdrawn.

Applicants kindly request reconsideration and allowance of the pending claims. If any issues remain, the Examiner is cordially invited to call Applicants' representative to discuss resolution thereof.

Respectfully submitted,



James E. Klaniecki
Registration No. 38,207

Immunex Corporation
51 University Street
Seattle, WA 98101
Telephone: (206) 265-4145
Facsimile: (206) 233-0644

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, Mail Stop RCE, P.O. Box 1450, Alexandria, VA 22313-1450, on the date indicated below.

Date: Feb. 2, 2004

Signed: 
Nanci M. Kertson